

WHAT IS CLAIMED IS:

1. A DNA construct comprising:
a first DNA segment encoding a precursor polypeptide comprising a pro-sequence of a mammalian t-PA; and
a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycoprotein.
2. The DNA construct of claim 1 wherein the heterologous glycoprotein is an immunoadhesin.
3. The DNA construct of claim 2 wherein the immunoadhesin is a TNF receptor immunoadhesin.
4. The DNA construct of claim 3 wherein the TNF receptor immunoadhesin is TNFR1-IgG1.
5. The DNA construct of claim 1 wherein the DNA encoding the mammalian t-PA pro-sequence is operably linked to a pre-sequence other than a mammalian t-PA pre-sequence.
6. The DNA construct of claim 5 wherein the heterologous glycoprotein is an immunoadhesin.
7. The DNA construct of claim 6 wherein the immunoadhesin is a TNF receptor immunoadhesin.
8. The DNA construct of claim 7 wherein the TNF receptor immunoadhesin is TNFR1-IgG1.
9. The DNA construct of claim 5 wherein the mammalian t-PA pro-sequence is operably linked a pre-sequence associated with the native heterologous polypeptide.
10. The DNA construct of claim 9 wherein the heterologous glycoprotein is a TNF receptor immunoadhesin and the pre-sequence is a pre-sequence of a mammalian TNF receptor.
11. The DNA construct of claim 10 wherein the mammalian t-PA pro-sequence is SEQ ID NO: 7.
12. The DNA construct of claim 11 wherein the pre-sequence is SEQ ID NO: 8.
13. The DNA construct of claim 12 wherein the TNF receptor immunoadhesin is TNFR1-IgG1.
14. A DNA construct comprising:
a first DNA segment encoding a precursor peptide; and
a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycosylation site variant glycoprotein.

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15. The DNA construct of claim 14 further comprising one or more additional DNA segments operably linked to the first and second DNA segments.

16. The DNA construct of claim 14 wherein the precursor peptide comprises the pro-sequence of a mammalian t-PA.

17. The DNA construct of claim 16 wherein the pro-sequence is a human t-PA pro-sequence.

18. The DNA construct of claim 17 wherein the pro-sequence is SEQ ID NO: 5.

19. The DNA construct of claim 16 further comprising a pre-sequence of a mammalia t-PA.

20. The DNA construct of claim 19 wherein the pre-sequence is a human t-PA pre-sequence.

21. The DNA construct of claim 20 wherein the pre-sequence is SEQ ID NO: 3.

22. The DNA construct of claim 21 wherein the precursor peptide is SEQ ID NO 1.

23. The DNA construct of claim 14 wherein the heterologous glycosylation site variant is a glycosylation site addition variant.

24. The DNA construct of claim 14 wherein the heterologous glycosylation site variant is a glycosylation site deletion variant.

25. The DNA construct of claim 24 wherein the heterologous glycosylation site variant is an immunoadhesin.

26. The DNA construct of claim 25 wherein the immunoadhesin is TNFR-IgG.

27. The DNA construct of claim 26 wherein the TNFR-IgG is TNFR1-IgG1.

28. The DNA construct of claim 27 wherein the TNFR1-IgG1 has an N-linked glycosylation site selected from the group consisting of amino acid positions 14, 105, 111 and 248 deleted.

29. The DNA construct of claim 28 wherein the TNFR1-IgG1 has the N-linked site at 14 deleted.

30. A cultured eukaryotic host cell comprising a DNA construct comprising:
a first DNA segment encoding a precursor peptide corresponding to a mammalian tissue plasminogen activator secretory peptide; and
a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycosylation site variant.

31. The cultured eukaryotic host cell of claim 30 wherein the host cell is a rodent host cell.

32. The cultured eukaryotic host cell of claim 31 which is a CHO cell.

33. A method of producing a polypeptide which has been altered to delete one or more native N-linked glycosylation sites comprising the steps of

(a) culturing a eukaryotic host cell comprising a DNA construct comprising:

a first DNA segment encoding a precursor peptide corresponding to a mammalian tissue plasminogen activator signal-pro peptide; and

a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycosylation site deletion variant polypeptide;

wherein the eukaryotic host cell express the first and second DNA segments and the polypeptide is secreted from the cell; and

(b) recovering the polypeptide so produced.